

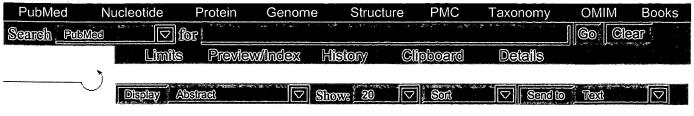
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Gastroenterology

Transforming growth factor beta type II receptor gene mutations in adenomas from hereditary nonpolyposis colorectal cancer.

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BACKGROUND & AIMS: Germline mutations of DNA mismatch repair genes are responsible for cancer susceptibility in hereditary nonpolyposis colorectal cancer (HNPCC) kindreds. Transforming growth factor beta type II receptor (TGF-beta RII) has been found to be somatically altered in HNPCC. The aim of this study was to clarify further the role of TGF-beta RII alterations in HNPCC tumorigenesis, particularly in adenomas. METHODS: Fourteen adenoma specimens and 13 cancer specimens from 10 patients with HNPCC were screened for mutations in the short repeated sequences of the TGF-beta RII gene by polymerase chain reaction-single-strand conformation polymorphism. Mismatch repair genes, replication errors, and c-K-ras 2 were also analyzed in HNPCC tumors. RESULTS: Alterations of the TGF-beta RII gene at the short poly(A) repeat were found in 8 (57%) adenoma specimens and 11 (85%) cancer specimens. They were found at an earlier stage of adenomas. Two adenoma specimens showed two-hit inactivation of mismatch repair genes. Replication errors were detectable in 13 (93%) adenoma specimens. Mutations in c-K-ras 2 codon 12 were detected at a 50% frequency in adenoma specimens. CONCLUSIONS: These data indicate a strong association between TGF-beta RII gene alterations and adenoma-carcinoma progression in HNPCC.

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